Environmental Health
PERSPECTIVES
Journal of the National Institute of Environmental Health Sciences

ehponline.org

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doi:10.1289/ehp.5756 (available at http://dx.doi.org/)
Online 6 December 2002

The National Institute of Environmental Health Sciences
National Institutes of Health
Department of Health and Human Services

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Running title: Phthalates and DNA damage in human sperm.

Keywords: Phthalates, urinary metabolites, environmental, DNA damage, comet assay, human sperm, specific gravity adjustment.

We acknowledge the National Institute of Environmental Health Sciences (Grant ES09718, ES00002). NIH Training grant T32 ES07069 supported S.Duty. We also thank Drs. Antonia Calafat, Zuying Chen, and Shanna Swan, also Janna Frelich, Linda Godfrey-Bailey, Alan Larson, Nelta Mercedat, Lucille Pothier, Ana Trisini, Peter Hengel and Impuls Bildanalyse GMBH, Germany.

List of abbreviations used in the manuscript:

MEHP = mono-2-ethylhexyl phthalate, MEP = monoethyl phthalate, MBP = mono-n-butyl phthalate, MBzP = monobenzyl phthalate, MMP = monomethyl phthalate, MINP = mono-3-methyl-5-dimethylhexyl (isononyl) phthalate, MOP = mono-n-octyl phthalate, MCHP = monocyclohexyl phthalate, DiBP = diisobutyl phthalate, DBP = di-n-butyl phthalate, BBzP = butyl benzyl phthalate, DEHP = di(2-ethylhexyl) phthalate, FISH = fluorescence in situ hybridization, TDM = tail distributed moment, IQR = interquartile range, TUNEL = terminal deoxynucleotidyl transferase-mediated dUTP-biotin end-labeling, SCSA = sperm chromatin structure assay, NHANES = National Health and Nutrition Examination Survey, PVC = polyvinyl chloride, BMI = body mass index, CASA = computer aided semen analysis, SAS = statistical analysis software, LOD = limit of detection, MGH = Massachusetts General Hospital, Tail % = percent DNA in tail, WHO = World Health Organization, HPLC = high performance liquid chromatography.

ABSTRACT

Phthalates are industrial chemicals widely used in many commercial applications. The general population is exposed to phthalates through consumer products as well as through diet and medical treatments. To determine whether environmental levels of phthalates are associated with altered DNA integrity in human sperm, we selected a population without identified sources of exposure to phthalates. One hundred and sixty eight subjects recruited from the Massachusetts General Hospital Andrology Laboratory provided a semen and urine sample. Eight phthalate metabolites were measured in urine by using high performance liquid chromatography and tandem mass spectrometry; data were corrected for urine dilution by adjusting for specific gravity. The neutral single cell microgel electrophoresis assay (Comet Assay) was used to measure DNA integrity in sperm. VisComet image analysis software was used to measure comet extent, a measure of total comet length (μm), percent DNA in tail (tail %), a measure of the proportion of total DNA present in the comet tail, and tail distributed moment (TDM), an integrated measure of length and intensity (μm). For an interquartile range increase in specific gravity-adjusted monoethyl phthalate (MEP) level, the comet extent increased significantly by 3.6 μm (95%CI: 0.74, 6.47); the TDM also increased 1.2 μm (95%CI: -0.05, 2.38), but was of borderline significance. Monobutyl, monobenzyl, monomethyl and mono 2-ethylhexyl phthalates, were not significantly associated with comet assay parameters. In conclusion, this study represents the first human data to demonstrate that urinary MEP, at environmental levels, is associated with increased DNA damage in sperm.